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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/937,181	01/10/2002	Geoffrey Phillip Dobson	FREE001	6148

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EXAMINER	
DAVIS, RUTH A	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 12/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/937,181	DOBSON, GEOFFREY PHILLIP	
	Examiner	Art Unit	
	Ruth A. Davis	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 September 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,44-81,84,86,87,89 and 91-106* is/are pending in the application.

4a) Of the above claim(s) *1-8,44-76* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *77-81,84,86,87,89 and 91-106* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group II, claims 77 – 93 in the Office action mailed on March 25, 2003 is affirmed. It is noted that Applicant has affirmed the election with traverse. Regarding the traverse, Applicant argues that a lack of unity was not made in the International Application, and therefore the present case should also have unity. However, this argument is not found persuasive because there is no special technical feature among the inventions which contribute over the prior art. In support, the cited reference teach compositions comprising pharmaceutical carriers; a potassium channel opener, an agonist thereof, or an adenosine receptor agonist; and a local anesthetic.

The requirement is still deemed proper and is therefore made FINAL.

It is noted:

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection

are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Claim Objections

Claim objections have been withdrawn due to amendment.

Claim Rejections - 35 USC § 112

Rejections under 35 U.S.C. 112, second paragraph have been withdrawn due to amendment.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims77 – 78, 80 – 81, 94 – 95, 97 – 98, 100 – 101, and 103 – 105 are rejected under 35 U.S.C. 102(b) as being anticipated by Antropoli.

Applicant claims composition comprising a pharmaceutical carrier; a compound selected from potassium channel opener, an agonist thereof, and an adenosine receptor agonist; and a local anesthetic. The compound and anesthetic are in amounts effective to arrest, protect or preserve the heart. The potassium channel opener or agonist thereof is selected from a named group; and the local anaesthetic is selected from mexiletine, diphenylhydantoin, prilocaine, procaine, mepivacaine and class 1B antiarrhythmic agents, specifically lignocaine. The composition is a cardioplegic or cardioprotectant composition.

Antropoli teaches compositions comprising nifedipine (potassium channel opener), and lidocaine (local anesthetic, class 1B antiarrhythmic agent, lignocaine) or carbocaine (local anesthetic) (abstract). The composition may further contain other drugs (abstract), carriers and excipients (claims).

Although Antropoli does not specifically teach the composition is a cardioplegic, the compositions are the same. Therefore, the composition of Antropoli must inherently act as a cardioplegic.

The reference anticipates the claimed subject matter.

4. Claims 77 – 78, 80 – 81, 93 – 95, 97 – 98, 100 – 101 and 103 – 105 are rejected under 35 U.S.C. 102(b) as being anticipated by Homeister.

Applicant claims composition comprising a pharmaceutical carrier; a compound selected from potassium channel opener, an agonist thereof, and an adenosine receptor agonist; and a local anesthetic. The compound and anesthetic are in amounts effective to arrest, protect or preserve the heart. The potassium channel opener or agonist thereof is selected from a named group, specifically AV blocker adenosine; and the local anaesthetic is selected from mexiletine, diphenylhydantoin, prilocaine, procaine, mepivacaine and class 1B antiarrhythmic agents, specifically lignocaine. The composition is a cardioplegic or cardioprotectant composition.

Homeister teaches compositions comprising adenosine and lidocaine (Class 1B antiarrhythmic, local anesthetic, lignocaine) for controlling myocardial injury (abstract) administered with saline (p.597).

Although Homeister does not specifically teach the composition is cardioplegic, the compositions are the same. Therefore, the composition of Homeister must inherently act as a cardioplegic.

The reference anticipates the claimed subject matter.

5. Claims 77 – 78, 80 – 81, 93 – 95, 97 – 98, 100 – 101 and 103 – 105 are rejected under 35 U.S.C. 102(b) as being anticipated by Garratt.

Applicant claims composition comprising a pharmaceutical carrier; a compound selected from potassium channel opener, an agonist thereof, and an adenosine receptor agonist; and a local anesthetic. The compound and anesthetic are in amounts effective to arrest, protect or preserve the heart. The potassium channel opener or agonist thereof is selected from a named group, specifically AV blocker adenosine; and the local anaesthetic is selected from mexiletine, diphenylhydantoin, prilocaine, procaine, mepivacaine and class 1B antiarrhythmic agents, specifically lignocaine. The composition is a cardioplegic or cardioprotectant composition.

Garratt teaches a composition of adenosine and lidocaine (Class 1B antiarrhythmic, local anesthetic, lignocaine) and it's benefit in patients with myocardial infarctions (abstract). Garratt teaches the addition of adenosine and lidocaine to cardioplegic solutions reduces ventricular dysfunction and has similar benefits for myocardial infarction (p.196). Other medicaments for managing myocardial infarction were (aspirin, beta-blockers) were co-administered (p.197).

The reference anticipates the claimed subject matter.

6. Claims 77 – 78, 80, 84, 86 – 87, 89, 94 – 95, 97, 99 – 101, 103 and 105 – 106 are rejected under 35 U.S.C. 102(b) as being anticipated by Jayawant.

Applicant claims composition comprising a pharmaceutical carrier; a compound selected from potassium channel opener, an agonist thereof, and an adenosine receptor agonist; and a local anesthetic. The compound and anesthetic are in amounts effective to arrest, protect or preserve the heart. The potassium channel opener or agonist thereof is selected from a named group; and the local anaesthetic is selected from mexiletine, diphenylhydantoin, prilocaine, procaine, mepivacaine and class 1B antiarrhythmic agents. The carrier comprises a buffer that maintains the pH of the composition at about 6 – 9, the potassium has a concentration of about 10 mM, the magnesium has a concentration of about 2.5 mM, and the buffer is selected from Krebs-Henseleit, St. Thomas No.2 solution, Tyrodes solutions, Fremes solution, Hartmanns solution of Ringers-Lactate. The composition is a cardioplegic or cardioprotectant composition.

Jayawant teaches cardioplegic compositions of Krebs-Henseleit and pinacidil, wherein the infusions contain procaine (abstract, p.133). Jaywant teaches pinacidil is administered with Krebs-Henseleit as a delivery medium (p.133).

Although Jayawant does not specifically teach the buffer has a pH of 6 – 9, the buffers used are those as claimed, therefore they must have a pH of 6 – 9. Furthermore, although Jayawant does not teach the compositions wherein the carrier has up to 10mM potassium or up to 2.5mM magnesium, Krebs-Henseleit was known to have these amounts of potassium and magnesium. (See Raymond US 5693462, Table 1.)

The reference anticipates the claimed subject matter.

Applicant argues the references above do not teach the claimed composition comprising a carrier, compound and anesthetic in amounts sufficient to arrest, protect and preserve the heart.

However, this argument fails to persuade because Antropoli clearly teaches carriers in the composition, as it is used in a gel (p.10, claims), Homeister teaches administering the composition in saline (p.597), Garratt administers the components via IV (abstract), and Jayawant specifically teaches a delivery medium of Krebs-Henseleit (abstract). Regarding the effective amounts, the claims do not require any particular amount of each component. Therefore, the reference compositions appear to be the same.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claim77 – 78, 80 – 81, 84, 86 – 87, 89, 94 – 95, 97 – 101, 103 – 106 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jayawant.

Applicant claims composition comprising a pharmaceutical carrier; a compound selected from potassium channel opener, an agonist thereof, and an adenosine receptor agonist; and a local anesthetic. The compound and anesthetic are in amounts effective to arrest, protect or preserve the heart. The potassium channel opener or agonist thereof is selected from a named

group; and the local anaesthetic is selected from mexiletine, diphenylhydantoin, prilocaine, procaine, mepivacaine and class 1B antiarrhythmic agents, specifically lignocaine. The carrier comprises a buffer that maintains the pH of the composition at about 6 – 9, the potassium has a concentration of about 10 mM, the magnesium has a concentration of about 2.5 mM, and the buffer is selected from Krebs-Henseleit, St. Thomas No.2 solution, Tyrodes solutions, Fremes solution, Hartmanns solution of Ringers-Lactate. The composition is a cardioplegic or cardioprotectant composition.

Jayawant teaches cardioplegic compositions of Krebs-Henseleit and pinacidil, wherein the infusions contain procaine (abstract, p.133). Jaywant teaches pinacidil is administered with Krebs-Henseleit as a delivery medium (p.133). Although Jayawant does not specifically teach the buffer has a pH of 6 – 9, the buffers used are those as claimed, therefore they must have a pH of 6 – 9. Furthermore, although Jayawant does not teach the compositions wherein the carrier has up to 10mM potassium or up to 2.5mM magnesium, Krebs-Henseleit was known to have these amounts of potassium and magnesium. In support, Raymond (US 5693462) teaches Krebs-Henseleit contains 3 – 30mM potassium and 0.9 – 4.8mM magnesium (Table 1).

Jayawant does not teach each of the claimed potassium channel openers, buffers or anesthetics in the compositions. However, Jayawant does teach that potassium channel openers, Krebs-Henseleit solution, and St. Thomas' Hospital solution are effective cardioplegic agents (p.132, abstract). Therefore, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by Jayawant to substitute other potassium channel openers, buffers and/or anesthetics in the disclosed composition with a reasonable expectation for successfully obtaining an effective cardioplegic composition.

9. Claims 77 – 78, 80 – 81, 91 – 95, 97 – 98, 100 – 101 and 103 – 105 are rejected under 35 U.S.C. 103(a) as being unpatentable over Garratt in view of Glasser.

Applicant claims composition comprising a pharmaceutical carrier; a compound selected from potassium channel opener, an agonist thereof, and an adenosine receptor agonist, specifically AV blocker adenosine; and a local anesthetic. The compound and anesthetic are in amounts effective to arrest, protect or preserve the heart. The potassium channel opener or agonist thereof is selected from a named group; and the local anaesthetic is selected from mexiletine, diphenylhydantoin, prilocaine, procaine, mepivacaine and class 1B antiarrhythmic agents, specifically lignocaine. The composition further comprises a medicament selected from dipyridamole and a clot busting drug, specifically spretokinase. The composition is a cardioplegic or cardioprotectant composition.

Garratt teaches a composition of adenosine and lidocaine (Class 1B antiarrhythmic, local anesthetic, lignocaine) and it's benefit in patients with acute myocardial infarctions (abstract). Garratt teaches the addition of adenosine and lidocaine to cardioplegic solutions reduces ventricular dysfunction and has similar benefits for myocardial infarction (p.196). Other medicaments for managing myocardial infarction were (aspirin, beta-blockers) were co-administered (p.197).

Garratt does not teach the compositions wherein the additional medicaments co-administered were dipyridamol or streptokinase. However, Glasser teaches that streptokinase is commonly used to treat acute myocardial infarction (col.9 line 5-12). At the time of the claimed invention, one of ordinary skill in the art would have been motivated by Glasser to combine

streptokinase to the composition of Garratt because of its known use in managing acute myocardial infarction. Further, it would have been obvious to one of ordinary skill in the art to combine streptokinase, adenosine and lidocaine for their common benefit as cited by the references above. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated to combine streptokinase, adenosine and lidocaine together with a reasonable expectation for successfully obtaining a composition effective for treating acute myocardial infarction.

10. Claims 77 – 81, 93 – 98 and 100 – 105 are rejected under 35 U.S.C. 103(a) as being unpatentable over Garratt or Homeister.

Applicant claims composition comprising a pharmaceutical carrier; a compound selected from potassium channel opener, an agonist thereof, and an adenosine receptor agonist, specifically AV blocker adenosine; and a local anesthetic. The compound and anesthetic are in amounts effective to arrest, protect or preserve the heart. The potassium channel opener or agonist thereof is selected from a named group; and the local anaesthetic is selected from mexiletine, diphenylhydantoin, prilocaine, procaine, mepivacaine and class 1B antiarrhythmic agents, specifically lignocaine. The composition is a cardioplegic or cardioprotectant composition.

Garratt teaches a composition of adenosine and lidocaine (Class 1B antiarrhythmic, local anesthetic) and it's benefit in patients with acute myocardial infarctions (abstract). Garratt teaches the addition of adenosine and lidocaine to cardioplegic solutions reduces ventricular

dysfunction and has similar benefits for myocardial infarction (p.196). Other medicaments for managing myocardial infarction (aspirin, beta-blockers) were co-administered (p.197).

Homeister teaches compositions comprising adenosine and lidocaine (Class 1B antiarrhythmic, local anesthetic) for controlling myocardial injury (abstract) administered with saline (p.597). Although Homeister does not specifically teach the composition is cardioplegic, the compositions are the same. Therefore, the composition of Homeister must inherently act as a cardioplegic.

The references do not teach the compositions wherein an adenosine receptor agonist is used. However, at the time of the claimed invention, it would have been obvious to one of ordinary skill in the art to use an analogue or agonist of adenosine in the reference compositions as a matter of routine experimentation. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by routine practice to use agonists/analogues of adenosine in the reference compositions with a reasonable expectation for successfully obtaining a composition effective for treating myocardial conditions.

Applicant argues the references do not alone or in combination teach or suggest the claimed composition for arresting, protecting or preserving the heart.

However, this argument fails to persuade because Jayawant specifically teaches a cardioplegic (heart stopping/arresting) composition comprising the compounds in combination with carriers and anesthetics. Garratt and Glasser teach the carriers, compounds, anesthetics and streptokinases were all know to treat acute myocardial infarction. Although the references may

not teach the claimed function as applicant, one of ordinary skill in the art would certainly have been motivated to combine the components together with a reasonable expectation for successfully obtaining an effective treatment for acute myocardial infarction. The intended use of the composition does not patentably distinguish the composition, per se, since such undisclosed use is inherent in the reference composition. Furthermore, Garratt and Homeister both teach compositions comprising adenosine and lidocaine (lignocaine) in pharmaceutical carriers. Although the references do not teach the effective amounts, it is noted that specific amounts are not required by the claims. Therefore, the reference compositions appear to be the same.

Conclusion

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruth A. Davis whose telephone number is 703-308-6310. The examiner can normally be reached on M-H (7:00-4:30); altn. F (7:00-3:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 703-308-0196. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Effective January 20, 2004, any inquires should be made to Ruth Davis whose telephone number is 571-272-0915. The examiner's supervisor, Michael Wityshyn, can be reached at 571-272-0926.

Ruth A. Davis; rad
December 8, 2003

LEON B. LANKFORD, JR.
PRIMARY EXAMINER